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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,792	10/26/2006	Hiroyuki Kamiya	2006_1315A	9531

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WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
PANDE, SUCHIRA	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,792	KAMIYA ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-22* is/are pending in the application.

4a) Of the above claim(s) *17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Examiner acknowledges election of Group I claims 12-16. Claims 17-22 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 10, 2007. Claims 12-16 are under examination and will be examined in this action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 12 recitation of non standard transition phrase ---- "characterized by"---- renders the claim indefinite. In the present form, the scope of the claimed invention is unclear to one of ordinary skill. Examiner suggests use of standard transitional phrase "comprising".

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grunert et al. (US pat. 6,010,908 issued Jan 4, 2000) in view of Moriya (1993) Proc. Natl. Acad. Sci. USA vol. 90 pp1122-1126 and Marron et al. (2000) Diabetes vol. 49: pp 492-499.

Regarding claim 12, Grunert et al. teach a base conversion method of a DNA sequence (see title where term gene therapy is used to teach a base conversion method of a DNA sequence),

which is a method of converting one or more bases in a target DNA sequence in a cell (see col. 4 lines 35-37 where small fragment homologous replacement (SFHR) of mutated gene sequences in vivo and vitro are taught. By teaching targeted SFHR of the mutated cystic fibrosis (CF) gene (see col. 4 lines 43-44) in a subjects's target cells,

Grunert et al. teach a method of converting one or more bases in a target DNA sequence in a cell)

characterized by introducing a single-stranded DNA fragment (see col. 54 lines 34-35 where 491 nucleotide single stranded DNA (ssDNA) is taught. See col. 54 lines 55-57 where electroporation is taught as a method to introduce the 491 nt. ssDNA into cells.

having 300 to 3,000 bases (by teaching 491 base ssDNA, Grunert et al. teach 300 to 3,000 bases)

is homologous with the target DNA sequence, and contains the base(s) to be converted, into a cell (the 491 base fragment was derived from a 860 bp fragment contained in CFTR exon 10, as well as 5' and 3' intron sequence. See col. 54 lines 10-20) thus the 491 base ssDNA is homologous with the target (CF) DNA sequence.

Regarding claim 12, Grunert et al. teach the formation of the ssDNA by denaturation of 491 bp DNA fragment obtained by PCR (see col. 54 lines 39-50).

Regarding claim 14, Grunert et al. teach, wherein the single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence (see col. 54 line 35 where 491 nt ss DNA fragment is used for homologous replacement. Since the ss DNA was made by denaturing the ds DNA therefore the mixture of ss DNA fragments contains both the sense and the antisense strand of the target DNA sequence. Therefore Grunert et al. teach, wherein the single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence.

Regarding claim 15, Grunert et al. teach wherein the target DNA sequence in the cell is a DNA sequence causing a disease due to the one or more bases (see col. 53 example 18 where target DNA taught is mutant CFTR which causes cystic fibrosis due to mutant CFTR gene. Thus teaching the target DNA sequence in the cell is a DNA sequence causing a disease due to the one or more bases).

Regarding claim 15, Grunert et al. teach, wherein one or more bases in a target DNA sequence in a cell of an organism are converted (See col. 56 lines 1-25 where homologous DNA replacement was confirmed by allele-specific southern hybridization).

Regarding claim 12, Grunert et al. do not teach single-stranded DNA fragment is prepared by cleavage from a single-stranded circular DNA,

Regarding claim 12, Moriya teaches single-stranded DNA fragment is prepared by cleavage from a single-stranded circular DNA (see page 1123 par. 1 where ss pMS2 phagemids (single stranded circular DNAs) are taught and enzyme EcoRV sal I are taught to cleave ss pMS2. Thus Moriya teaches single-stranded DNA fragment is prepared by cleavage from a single-stranded circular DNA.

Regarding claim 13, Moriya teaches wherein the single-stranded circular DNA is a phagemid DNA (ss pMS2 is taught as a phagemid see above).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Moriya in the method of Grunert et al. The motivation to do so is provided to one of ordinary skill in the art both by teachings of Moriya as well as knowledge of the art itself.

Moriya states "It is concluded that a single—stranded shuttle vector, utilized in conjunction with a site-specific approach, can be used to investigate translesional events in mammalian cells and in bacteria". (see page 1122 end of abstract).

Thus by above teaching of Moriya one of ordinary skill knows that phagemids (ss DNA vector pMS2 derived from the pSVK3 backbone sold by Pharmacia—see page 1122 materials and method section) taught by Moriya can be used to generate single stranded DNA fragments that can be introduced into mammalian cells.

Grunert et al. teach a method using which they were able to convert one or more bases of CFTR mutated gene in a cell to alleviate the symptoms of CFTR, one of ordinary skill can envisage applying the method to various other diseases that are caused by known genetic lesions.

One of ordinary skill knows that if they want to target the coding sequence for human gene intended for alteration then they need to introduce a single stranded DNA that is homologous with a sense strand of the target DNA sequence.

100 kb Phagemid artificial chromosomes (Marron et al. 2000) that contain Type I Diabetes susceptibility gene (IDDM12) was taught to one of ordinary skill by prior art at the time of the invention. Hence one ordinary skill would be motivated to subclone the (IDDM12) gene from the above 100 kb construct into phagemid vectors taught by Moriya such that the ssDNA produced is homologous with a sense strand of the target (IDDM12) gene. By using the phagemid shuttle vectors not only are they able to propagate and amplify these clones in bacteria, but also obtain a pure single stranded DNA substrate containing the desired DNA strand without requiring additional steps of

PCR amplification followed by denaturation where only 50% of the strands will have the desired sequence. The resulting method is both faster and cleaner method. In addition such a method will produce 100 % ssDNA of desired sequence. These ssDNA circular DNA, can be cleaved by restriction enzymes to provide fragments, which can be used in the gene therapy protocols.

Conclusion

7. All elected claims 12-16 are rejected over prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

2/7/08